

WHAT IS CLAIMED IS:

1. A method of preventing or treating lytic bone disease in a mammal comprising administering a therapeutically effective amount of an OPG polypeptide.

2. A method for preventing the metastasis of cancer to bone comprising administering a therapeutically effective amount of an OPG polypeptide.

3. A method for preventing the osteosclerotic bone metastasis comprising administering a therapeutically effective amount of an OPG polypeptide.

4. The method of Claim 1 or 2 or 3 further comprising administering a therapeutically effective amount of a cancer therapy agent.

5. The method of Claims 1 or 2 or 3 or 4 wherein the OPG polypeptide comprises an amino acid sequence as shown in Figure 2 (SEQ ID NO: 2) or a truncated polypeptide thereof.

6. The method of Claim 4 wherein the OPG polypeptide comprises a carboxy terminal truncation of part or all of amino acid residues 186-401 as shown in Figure 2 (SEQ ID NO: 2).

7. The method of Claim 4 wherein the OPG polypeptide comprises amino acid residues 22-194 inclusive as shown in Figure 2 (SEQ ID NO: 2).

8. The method of Claims 5, 6 or 7 wherein the OPG polypeptide is an OPG fusion polypeptide.

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9. The method of Claim 8 wherein the OPG fusion polypeptide comprises a fusion of an Fc region to the N-terminal or C-terminal end of the OPG polypeptide.

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10. The method of Claim 9 wherein the OPG fusion polypeptide comprises an Fc region fused to amino acid residues 22-194 of Figure 2 (SEQ ID NO: 2).

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11. The method of Claim 10 wherein the OPG fusion polypeptide consists of the amino acid sequence as shown in Figure 5 or in Figure 8 (SEQ ID NO: 5 or 8).

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12. The method of Claim 1 or 2 or 3 wherein the OPG polypeptide is administered prior to, concurrent with, or subsequent to administration of a cancer therapy agent.

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13. The method of Claim 1 or 3 wherein lytic bone disease occurs in conjunction with cancer which has metastasized to bone.

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14. The method of Claim 13 wherein the cancer is selected from the group consisting of breast cancer, prostate cancer, thyroid cancer, cancer of the kidney, lung cancer, esophageal cancer, rectal cancer, bladder cancer, cervical cancer, ovarian cancer, liver cancer, cancer of the gastrointestinal tract, multiple myeloma, and lymphoma.

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15. The method of Claim 1 or 2 or 3 wherein the cancer therapy agent is selected from the group consisting of radiation, chemotherapy, antibodies, or non-antibody polypeptides.

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16. The method of Claim 15 wherein chemotherapy comprises anthracyclines, taxol, tamoxifene, doxorubicin, and 5-fluorouracil.

5 17. The method of Claim 15 wherein the antibodies bind to Her2, CDC20, CDC33, mucin-like glycoprotein, or epidermal growth factor receptor (EGFR) on the surface of tumor cells.

10 18. The method of Claim 15 wherein the cancer therapy agent comprises a luteinizing hormone-releasing hormone (LHRH) antagonist.

15 19. The method of Claim 18 wherein the LHRH antagonist comprises the following structure:

A-B-C-D-E-F-G-H-I-J

wherein

A is pyro-glu, Ac-D-Nal, Ac-D-Qal; Ac-Sar, or Ac-D-Pal;

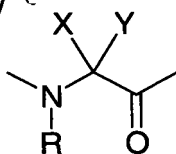
20 B is His or 4-Cl-D-Phe;

C is Trp, D-Pal, D-Nal, L-Nal-D-Pal(N-O), or D-Trp;

D is Ser;

25 E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is



30 wherein R and X are independently, H and alkyl; and Y comprises a small polar entity.

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg;

I is Pro; and

20. The method of Claim 18 wherein the LHRH antagonist comprises the peptide: N-Ac-D-Nal-4-Cl-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH<sub>2</sub>.

22. A method of preventing or treating multiple myeloma comprising administering therapeutically effective amount of an OPG polypeptide.

Add B<sup>8</sup>  
 Add  
 D<sup>2</sup>  
 Add  
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